

### **REMARKS/ARGUMENTS**

Claims 1-9 are pending in the captioned application and stand rejected.

Applicants have amended claims 1-3 and cancelled claims 5 and 9. Applicants respectfully submit that the amendments are fairly based on the specification and do not introduce new matter.

The specification stands objected to for failing to comply with the sequence listing rule. Specifically, there is a nucleic acid sequence on pages 15 and 16 that lack a sequence identifier. In response, Applicants have amended the specification and also provide the Sequence Listing with the instant response. Applicants submit that the objection should now be withdrawn.

Claim 2 stands objected to because the Examiner regards the claim language as unclear. In response, Applicants have amended this claim, adopting the Examiner's suggested language, i.e. "the biological solution is a synthesis reaction of antisense oligonucleotides". The claim objection should now be withdrawn.

Claim 3 stand objected to because the Examiner regards the claim language as unclear. In response, Applicants have amended this claim, making clear that the claim adds a further limitation that the "fully thioated antisense oligonucleotides are separated from incorrectly synthesised oligonucleotides". Applicants submit that in view of this amendment, the claim objection should now be withdrawn.

Claim 9 stands rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The claim is also rejected under 35 U.S.C. §101. In response, Applicants have cancelled the claim, rendering the rejection moot.

Claims 1-8 stand rejected under 35 U.S.C. §112, first paragraph, as being not fully enabled. Applicants respectfully disagree.

The Examiner acknowledges that the claims are enabled for separation of fully thioated antisense oligonucleotides from incorrectly thioated or incorrectly synthesised oligonucleotides using  $\text{Fe}^{3+}$  or  $\text{Zr}^{2+}$  IMAC resins and the buffer conditions described in the working examples. However, the Examiner regards the claims as not enabling for use of any metal ion and any eluent conditions to separate fully thioated antisense oligonucleotides from incorrectly thioated or incorrectly synthesised oligonucleotides.

In response, Applicants have amended the claims, including the limitation of using  $\text{Fe}^{3+}$  or  $\text{Zr}^{2+}$  IMAC resins in claim 1. Applicants submit that the claims as amended are enabled and the rejection should be withdrawn. Applicants submit that as amended, the claimed methods only relate to the use of  $\text{Fe}^{3+}$  or  $\text{Zr}^{2+}$  IMAC resins for the isolation of fully thioated single stranded antisense oligonucleotides. The specification clearly teaches that both metal ions are useful for such separation, as presented in the specification, including the examples, and acknowledged by Examiner.

Applicants further submit that the specification teaches elution of desired antisense oligonucleotides using standard methods, such as an increase in the pH


and/or phosphate gradient (page 12, lines 5-7). The Examples set forth in the specification further supports Applicants' assertion. Applicants submit that a skilled person in chromatography, provided with the teaching of the specification, would know how to use the invention. Based on the teaching of the instant specification, any experimentation needed for optimizing an elution condition would only be limited, and no undue experimentation is necessary. Therefore, Applicants submit that the amendment rejection should now be withdrawn.

Applicants respectfully request reconsideration and allowance of claims 1-4 and 6-8.

Early and favorable consideration is respectfully requested.

Respectfully submitted,

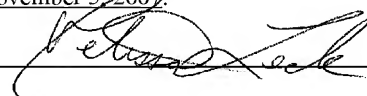
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